The University of Vermont
HUMAN BEHAVIORAL PHARMACOLOGY LABORATORY
DEPARTMENT OF PSYCHIATRY
38 FLETCHER PLACE – IRA ALLEN SCHOOL
BURLINGTON, VERMONT 05401-1419
TELEPHONE: (802) 656-9610
FAX: (802) 656-9628

July 14, 1999

Michael Friedman, M.D.
Lead Deputy Commissioner
Food and Drug Administration
5600 Fishers Lane, Room 1471
Rockville, MD 20857

Dear Dr. Friedman:

Re: Docket # 97 P-0498/CP-1

On July 7, 1997, I sent a petition to you to consider caffeine labeling. Then I sent a revision on November 20, 1997 (enclosed). I sent a request for a status update on August 7, 1998, but had no response. I sent another request on April 30, 1999 with no response. It is now 24 months since I submitted this petition.

Please write me with the status of this petition.

Sincerely,

John R. Hughes, M.D.
Professor

Enclosure

cc: Patricia Lieberman
Roland Griffiths, Ph.D.
Avram Goldstein, Ph.D.
Sean Donohue

The University of Vermont

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August 7, 1998

Sen. James Jeffords
Senate Labor Committee
428 Dirksen Senate Office
Washington, DC 20510

Dear Sen. Jeffords:

Enclosed are copies of a petition I submitted (along with 21 other scientists) over one year ago to the FDA about caffeine labeling. Despite repeated inquiries we have had no response from FDA. I am reluctant to take up your valuable time with this, but I would appreciate any inquiry you (or Sharon Winn) could make into this.

Sincerely,

John R. Hughes, M.D.
Professor

The University of Vermont

HUMAN BEHAVIORAL PHARMACOLOGY LABORATORY
DEPARTMENT OF PSYCHIATRY
38 FLETCHER PLACE — IRA ALLEN SCHOOL
BURLINGTON, VERMONT 05401-1419
TELEPHONE: (802) 660-3060
FAX: 802-660-3064

July 7, 1997

Michael Friedman, MD
Lead Deputy Commissioner
Food and Drug Administration
5600 Fishers Lane, Room 1471
Rockville MD 20857

Dear Dr. Friedman,

We are scientists who have extensively researched the behavioral effects of caffeine. We are writing to petition the FDA to include information on caffeine content in the labeling of foods and beverages. Our petition is based on recent evidence of the adverse behavioral effects of caffeine including the possibility of dependence.

Specifically, we recommend that all foods and beverages (including coffees, teas and sodas) which contain more than 5 mg of caffeine per serving include a statement of the mg of caffeine per serving.

The rationale for this recommendation is threefold: 1) caffeine can and does produce behavioral problems in adults and children, 2) caffeine use is ubiquitous, and 3) many consumers wish to know caffeine levels.

Behavioral Harm From Caffeine

Recent evidence has confirmed clinical observations that caffeine can induce anxiety, insomnia, intoxication (restlessness, difficulty concentrating, etc) and withdrawal (headaches, drowsiness, fatigue, etc.) (1,2). In fact, in some individuals, anxiety can occur with use of as little as 250 mg of caffeine (3) and withdrawal with as little as 100 mg/day (4). That caffeine can induce these problems is based on multiple well-controlled scientific studies (5,6). For example, caffeine can induce true panic attacks requiring medical treatment in susceptible individuals (6). The evidence of behavioral harm is sufficient such that it is recognized by the American Psychiatric Association in its DSM-IV official nomenclature (7) and in almost all standard medical textbooks.

Behavioral problems from caffeine are not rare. In one population-based study of adults (8), 30% of users reported caffeine-induced anxiety in the last year and 39% reported caffeine-induced insomnia. Of those who stopped caffeine use, 24% reported meeting the full DSM-IV criteria for a withdrawal syndrome.

Behavioral problems from caffeine are not confined to adults. Several experimental studies have demonstrated that some doses of caffeine can cause anxiety and restlessness in children (9). In addition, caffeine may have dependence potential in children (10,11). In one study, several children repeatedly chose caffeinated sodas in preference to uncaffeinated sodas in double-blind tests (11). The caffeinated and noncaffeinated sodas did not differ in taste tests; thus, it is clear these children were using the sodas for the pharmacological effects of caffeine. In another study, when 6-12 year old children abruptly stopped caffeine, their ability to attend to a task worsened and they developed headaches (10).

Prevalence of Caffeine Use

Caffeine is the most widely used psychoactive drug in the U.S. (12). It is also the only pharmacologically active and psychoactive substance permitted to be added to foods and beverages. The usual dose of caffeine from brewed coffee is approximately 100 mg/6 oz serving, from tea is 40 mg/6 oz serving and from soda is 40 mg/12 oz serving (12).

In the most recent surveys (12,13), 83% of adults report currently using caffeine with a mean intake of 200-250 mg/day among users. Among children, in the last nationwide survey (14), 98% consumed caffeine in the last week. The mean caffeine intake among children is low (1.0 mg/kg/day compared to 3.0 mg/kg/day in adults); however, there are some children with relatively high intakes (12). Coffee remains the greatest contributor of caffeine intake in adults (12); however, there has been a dramatic increase in caffeinated soda use in adults the last 20 years (15). Sodas are the major source of caffeine for children (15)

It is important to recognize the ubiquity of caffeine use for two reasons. First, the widespread use of caffeine makes it similar to protein, fat, cholesterol, carbohydrates and other currently labeled food ingredients in that it is consumed daily by almost the entire population. Second, the public health importance of exposure to a substance is the product of its impact and its degree of exposure. Thus, for example, a caffeine-induced problem that occurs in only 5% of users will still affect some 10 million consumers (1).

Public Interest in Caffeine Contents

The public's interest in the caffeine content of beverages and foods has increased substantially in the last decade. This is best illustrated by substantial sales of decaffeinated coffees and teas and noncaffeinated sodas; e.g., about 15% of coffee (12) and 30% of soda sales (Adamson, D., personal communication, 1995) are noncaffeinated. In addition, several "lite" coffees with "half" the usual caffeine content have been marketed without actual statements of caffeine amounts. Finally, new clear caffeinated waters can easily be mistaken for being caffeine-free. In summary, the market is changing such that simply listing the presence/absence of caffeine in fine print in a list of many other ingredients is insufficient. It is ironic that many consumers are choosing foods based on caffeine content but cannot discern how much caffeine is in them whereas consumers rarely choose foods based on their vitamin content but can find their vitamin contents on every food.

Our Recommendation

We are suggesting 5 mg per serving as the dose of caffeine in a food at which labeling should occur. Recent evidence indicates doses as low as 10 mg can produce mood changes that are discriminated by humans (16) and doses as low as 25 mg can induce caffeine self-administration (17); i.e., use of a beverage for the effect of caffeine. Thus, repeated doses of 5 mg could produce pharmacological effects. Although serving sizes vary across foods and beverages, we would note that although the industry has used 5 oz as a serving size for caffeinated beverages, 7-8 oz is a much more common serving size (12).

Summary

In summary, we believe the well-accepted evidence that caffeine can cause behavioral harm, the widespread use of caffeine, and the public's interest in knowing the caffeine content of their foods are compelling arguments that FDA should provide consumers with the caffeine content of all caffeine-containing foods and beverages.

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1. James JE, Understanding caffeine. Thousand Oakes, CA, Sage Publications, Inc. 1997.
2. Strain EC, Griffiths RR. Caffeine use disorders, in Psychiatry. Edited by Tasman A, Kay J, Lieberman JA. Philadelphia, W.B. Saunders Company, 1997.
3. Beck JG, Berisford. The effects of caffeine on panic patients: Response components of anxiety. Behav Ther 1992;405-422.
4. Griffiths RR, Evans SM, Heishman SJ, Preston KL, Sannerud CA, Wolf B, Woodson PP. Low-dose caffeine physical dependence in humans. J Pharmacol Exp Ther 1990;255:1123-1131.
5. Griffiths RR, Mumford GK. Caffeine--A drug of abuse? in Psychopharmacology: The Fourth Generation of Progress. Edited by Bloom FE, Kupfer DJ. New York, Raven Press, 1994.
6. Uhde TW. Caffeine provocation of panic: A focus of biological mechanism, in Neurobiology of Panic Disorder. Edited by Ballinger JC. New York, Alan R. Liss, Inc. 1990.
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8. Hughes JR, Oliveto AH, Bickel WK, Helzer JE, Higgins ST. Indicators of caffeine dependence in a population-based sample, in Problems of Drug Dependence, 1992. NIDA Research Monograph Series. Edited by Harris LS. Washington, US Gov't Printing Office, 1993.
9. Bernstein GA, Carroll ME, Crosby RD, Perwien AR, Go FS, Benowitz NL. Caffeine effects on learning, performance, and anxiety in normal school-age children. J Am Acad Child Adolesc Psychiatry 1994;33:407-415.

10. Bernstein GA, Walters N, Crosby R, Perwien A, Carroll M, Benowitz N. Caffeine withdrawal and the effects in normal children, in Scientific Proceedings 43rd Annual Meeting of the American Academy of Child and Adolescent Psychiatry Philadelphia, 1996.
11. Hale KL, Hughes JR, Oliveto AH, Higgins ST. Caffeine self-administration and subjective effects in adolescents. Exp Clin Psychopharm 1995;3:364-370.
12. Barone JJ, Roberts HR. Caffeine consumption. Food Chem Toxicol 1996;34:119-129.
13. Hughes JR, Oliveto AH. A systematic survey of caffeine intake in Vermont. Exp Clin Psychopharm, in press.
14. Morgan KJ, Stults VJ, Zabik ME. Amount and dietary sources of caffeine and saccharin intake by individuals ages 5 to 18 years. Regul Tox Pharmacol 1982;2:296-307.
15. Liebman B. The changing american diet. Nutrition Action Newsletter 1997;8-9.
16. Griffiths RR, Evans SM, Heishman SJ, Preston KL, Sannerud CA, Wolf B, Woodson PP. Low-dose caffeine discrimination in humans. J Pharmacol Exp Ther 1990;252:970-978.
17. Hughes JR, Oliveto AH, Bickel WK, Higgins ST, Badger GJ. The ability of low doses of caffeine to serve as reinforcers in humans: A replication. Exp Clin Psychopharm 1995; 3:358-363.

John R. Hughes, M.D.
Professor, Dept of Psychiatry
Dept. of Psychiatry
University of Vermont

Roland R. Griffiths, Ph.D.
Professor
Depts. of Psych and Neuroscience
Johns Hopkins University

Avram Goldstein, M.D.
Professor Emeritus
Dept. of Pharmacology
Stanford University

Enclosed are signatures of other scientists who agree with our petition.

If you have questions about this proposal, please contact John R. Hughes, M.D. via phone: (802)660-3065; Fax: (802)660-3064, email: john.hughes@uvm.edu or mail: Human Behavioral Pharmacology Lab, University of Vermont, 38 Fletcher Place, Burlington, Vermont 05401-1419.

We understand the Center for Science in the Public Interest will also be sending a petition on caffeine to you in the next few weeks. We would like our petition to be considered along with this. We would appreciate a written response to our proposal to be forwarded to Dr. Hughes after receipt of the CSPI paper.

Name	Title	Department	Affiliation	City	State	Fax Number
Neal Benowitz, Ph.D.	Professor	Psychiatry	San Francisco General Hospital	San Francisco	CA	4152064956
Gail Bernstein, M.D.	Associate Professor	Psychiatry	University of Minnesota Med School	Minneapolis	MN	6126265591
Marilyn Carroll, Ph.D.	Professor	Psychiatry	University of Minnesota	Minneapolis	MN	6126248935
Suzette Evans, Ph.D.	Assistant Professor	Psychiatry	NY State Psychiatric Institute	New York	NY	2127958860
Jack E. Henningfield, Ph.D.	Professor		Pinney Associates, Inc.	Bethesda	MD	3017180034
Frank Holloway, Ph.D.	Professor	Psychiatry & Behavioral Science	Univer of Oklahoma Hlth Sciences Ctr	Oklahoma City	OK	40527[illegible]2356
Steve Holtzman, Ph.D.	Professor	Pharmacology	Emory University School of Medicine	Atlanta	GA	4047270365
Leonard Howell, Ph.D.	Research Scientist	Pharmacology	Emory University School of Medicine	Atlanta	GA	4047271266
Jack James, Ph.D.	Professor	Psychology	LaTrobe University	Australia		01161394791783
Lynn T. Kozlowski, Ph.D.	Professor	Behavioral Health	Pennsylvania State University	University Park	PA	8148637525
James D. Lane, Ph.D.	Associate Research Professor	Psychiatry & Behavioral Health	Duke University Medical Center	Durham	NC	9196848629
Anthony Liguori, Ph.D.	Assistant Professor	Physiology & Pharmacology	Bowman Gray School of Medicine	Winston-Salem	NC	9107168501
Alison Oliveto, Ph.D.	Assistant Professor	Psychiatry	VA Medical Center	West Haven	CT	2039373478
John D. Roache, Ph.D.	Associate Professor	Psychiatry	Psychiatry Mental Science	Houston	TX	7137941425
Jed E. Rose, Ph.D.	Chief	Nicotine Research Lab	Veterans Administration Medical Ctr	Durham	NC	9192861388
Craig Rush, Ph.D.	Assistant Professor	Psychiatry & Human Behavior	University of Mississippi Medical Ctr	Jackson	MS	6019845885
Kenneth Silverman, Ph.D.	Assistant Professor	Psychiatry & Human Behavior	Johns Hopkins University	Baltimore	MD	4105501483
Roger D. Spealman, Ph.D.	Professor	Behavioral Biology	NE Regional Primate Research Ctr	Southborough	MA	5086248197
Eric Strain, M.D.	Assistant Professor	Behavioral Pharmacology	Biobehavioral Biology Research Ctr	Baltimore	MD	4105500030
Thomas W. Uhde, M.D.	Professor	Psychiatry	Wayne State University	Detroit	MI	3135775900
Philip Woodson, Ph.D.	Doctor of Natural Science		Intelligentsia, Inc.	Upper Montclair	NJ	2017468322

The University of Vermont

November 20, 1997

HUMAN BEHAVIORAL PHARMACOLOGY LABORATORY
DEPARTMENT OF PSYCHIATRY
38 FLETCHER PLACE — IRA ALLEN SCHOOL
BURLINGTON, VERMONT 05401-1419
TELEPHONE: (802) 660-3060
FAX: 802-660-3064

Jennie C. Butler, Chief
Dockets Management Branch
Department of Health and Human Services
Food and Drug Administration
Rockville, MD 20857

Dear Ms. Butler,

The following is a revision of the petition we submitted so that it conforms to the FDA regulations:

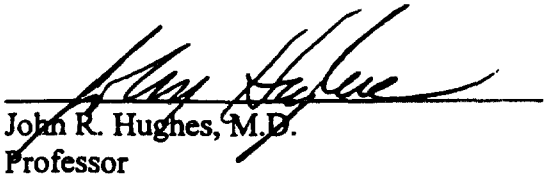
The undersigned (see attached names) submit this petition to request the Commissioner of Food and Drugs to "recommend that all foods and beverages (including coffees, teas and sodas) which contain more than 5 mg of caffeine per serving include a statement of the mg of caffeine per serving." (p 1 of prior letter).

The statement of grounds is included in the paragraphs labeled "Behavioral Harm from Caffeine," "Prevalence of Caffeine Use," and "Public Interest in Caffeine Contents."

We claim a categorical exclusion under section 25.24 to filing an environmental impact statement.

The undersigned certifies, that, to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petitioner which are unfavorable to the petition.

Signature



John R. Hughes, M.D.
Professor
Departments of Psychiatry, Psychology and Family Practice
38 Fletcher Place
Burlington, VT 05401-1419

cc: Patricia Lieberman, Ph.D.
Roland Griffiths, Ph.D.

The University of Vermont

HUMAN BEHAVIORAL PHARMACOLOGY LABORATORY
DEPARTMENT OF PSYCHIATRY
38 FLETCHER PLACE – IRA ALLEN SCHOOL
BURLINGTON, VERMONT 05401-1419
TELEPHONE: (802) 656-9610
FAX: (802) 656-9628

April 30, 1999

Michael Friedman, M.D.
Lead Deputy Commissioner
Food and Drug Administration
5600 Fishers Lane, Room 1471
Rockville, MD 20857

Dear Dr. Friedman:

Re: Docket # 97 P-0498/CP-1

On July 7, 1997, I sent a petition to you to consider caffeine labeling. Then I sent a revision on November 20, 1997 (enclosed). I sent a request for a status update on August 7, 1998, but had no response. It is now 20 months since I submitted this petition. Please write me with the status of this petition.

Sincerely,

John R. Hughes, M.D.
Professor

Enclosure

cc: Patricia Lieberman
Roland Griffiths, Ph.D.
Avram Goldstein, Ph.D.
Sean Donohue

00321

ROUTING SLIP
GENERATED BY: HF-40
DATE: MAY 10, 1999

FDA CONTROL NUMBER: 99 3121 **TRACER #:** **OS #:**

DATE OF CORRESPONDENCE: 04/30/99 **DATE INTO FDA:** 05/10/99

TO: MICHAEL A FRIEDMAN HF-28

FROM: JOHN R HUGHES, THE UNIVERSITY OF VERMONT

SYNOPSIS: REQUESTING INFORMATION ON THE STATUS OF CAFFEINE LABELING PETITION (DOCKET 97P-0498).

LEAD OFFICE: HFS-1 **HOME OFFICE:** HF-40

CONTACT/PHONE#: INDYA P GORDON 301-827-4440

COPIES: HF-28 MICHAEL A FRIEDMAN
HF-22
HF-40 VICTORIA B WOLFHARD
HFS-22 CATHERINE J BAILEY
HFA-305

COORDINATION:

SIGNATURE REQUIRED:

REFERRALS FROM HF-40

ASSIGNED TO		ACTION	DUE DATE
HFS-1	LEVITTJ	PREPARE DIRECT REPLY	06/10/99

REMARKS: PLEASE SEND COPY OF RESPONSE TO INDYA GORDON, HF-40, EXEC SEC.
98-6135/AUG. 31, 1998 (LATEST RESPONSE) LETTER IS ATTACHED.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

Mail copy to Roland Griffiths,
Carolyn Goldstein &
Patty Lieberman

December 02, 1997

John R. Hughes, M.D., Professor
University of Vermont
Human Behavioral Pharmacology Laboratory
Department of Psychiatry
38 Fletcher Place
Ira Allen School
Burlington, VT 05401-1419

Dear Dr. Hughes:

Your petition requesting the Food and Drug Administration to label all foods and beverages (including coffees, teas and sodas) which contain more than than 5mg caffeine per serving was received and completed by this office on 12/01/97. It was assigned docket number 97P-0498/CP 1 and it was filed on 12/01/97. Please refer to this docket number in future correspondence on this subject with the Agency.

Please note that the acceptance of the petition for filing is a procedural matter in that it in no way reflects an agency decision on the substantive merits of the petition.

Sincerely,

Jennie C Butler

Jennie Butler
Dockets Management Branch

The University of Vermont

November 20, 1997

HUMAN BEHAVIORAL PHARMACOLOGY LABORATORY
DEPARTMENT OF PSYCHIATRY
38 FLETCHER PLACE — IRA ALLEN SCHOOL
BURLINGTON, VERMONT 05401-1419
TELEPHONE: (802) 660-3060
FAX: 802-660-3064

Jennie C. Butler, Chief
Dockets Management Branch
Department of Health and Human Services
Food and Drug Administration
Rockville, MD 20857

Dear Ms. Butler,

The following is a revision of the petition we submitted so that it conforms to the FDA regulations:

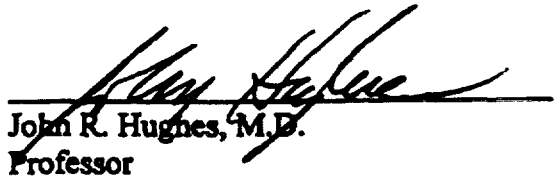
The undersigned (see attached names) submit this petition to request the Commissioner of Food and Drugs to "recommend that all foods and beverages (including coffees, teas and sodas) which contain more than 5 mg of caffeine per serving include a statement of the mg of caffeine per serving." (p 1 of prior letter).

The statement of grounds is included in the paragraphs labeled "Behavioral Harm from Caffeine," "Prevalence of Caffeine Use," and "Public Interest in Caffeine Contents."

We claim a categorical exclusion under section 25.24 to filing an environmental impact statement.

The undersigned certifies, that, to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petitioner which are unfavorable to the petition.

Signature



John R. Hughes, M.D.
Professor
Departments of Psychiatry, Psychology and Family Practice
38 Fletcher Place
Burlington, VT 05401-1419

cc: Patricia Lieberman, Ph.D.
Roland Griffiths, Ph.D.

98-615

AUG 31 1998

John R. Hughes, M.D.
Professor, Dept of Psychiatry
Human Behavioral Pharmacology Laboratory
University of Vermont
38 Fletcher Place
Burlington, VT 05401-1419

Re: Docket No. 97P-0498/CP1

Dear Dr. Hughes:

This letter is in further response to your citizen petition dated July 31, 1997, modified on November 20, 1997 and filed December 1, 1997 with the Food and Drug Administration (FDA) and your letter of August 7, 1998. Your petition was co-signed by Dr. Roland R. Griffiths of John Hopkins University and Dr. Avram Goldstein of Stanford University and was supported by various other individuals. Your petition requests that, based on recent evidence of the adverse behavioral effects of caffeine, the milligram amount of caffeine be required on the label of foods containing more than 5 mg of caffeine per serving.

In accordance with 21 CFR 10.30(e), this letter is to advise you that the FDA has not reached a decision on your petition within the first 180 days of its receipt. The petition raises complex issues that you contend support a requirement for quantitative disclosure of caffeine on food labels. The agency has not yet completed its evaluation of the information associated with your concerns. As soon as our evaluation is complete, we will notify you of the decision.

Sincerely yours,

Elizabeth Campbell

Elizabeth J. Campbell
Acting Director
Office of Food Labeling
Center for Food Safety
and Applied Nutrition

ROUTING SLIP
GENERATED BY: HF-40
DATE: JUL 21, 1999

FDA CONTROL NUMBER: 99 4786 **TRACER #:** **OS #:**

DATE OF CORRESPONDENCE: 07/14/99 **DATE INTO FDA:** 07/21/99

TO: MICHAEL FRIEDMAN, FDA

FROM: JOHN R HUGHES, THE UNIVERSITY OF VERMONT

SYNOPSIS: REQUESTING INFORMATION ON THE STATUS OF CAFFEINE LABELING PETITION (DOCKET 97P-0498)

LEAD OFFICE: HFS-1 **HOME OFFICE:** HF-40

CONTACT/PHONE#: STEVEN O SMITH 301-827-4450

COPIES: HF-22
HF-40 VICTORIA B WOLFHARD
HFS-22 CATHERINE J BAILEY
HFA-305

COORDINATION: --

SIGNATURE REQUIRED:

REFERRALS FROM HF-40

ASSIGNED TO		ACTION	DUE DATE
HFS-1	LEVITTJ	PREPARE RESPONSE FOR SIGNATURE	08/21/99

REMARKS: REFERENCE TRAC# 99 3121 (STILL PENDING) 98 6135 IS LATEST RESPONSE. PLEASE SEND COPY OF RESPONSE TO STEVE SMITH HF-40.